

**CONFIDENTIAL MATERIAL**

THE UNIVERSITY OF BIRMINGHAM  
BIOMEDICAL ETHICAL REVIEW SUB-COMMITTEE (BERSC)

25<sup>th</sup> May 2017

**MINUTES**

Present:

17/05-01            Apologies

17/05-02            Minutes

The minutes of the meeting held on 13<sup>th</sup> April 2017 were considered by the Committee and were approved subject to minor amendments.

17/05-03            Matters Arising

The SOP for the new intravital suite has been signed off and the suite is now operational. An induction programme for users of the suite has been developed.

It was reported that the anticipated visits to campus by the group Birmingham Animal Action did not occur.

17/05-04            Chairperson's Items

There were no Chairperson's items to report.

17/05-05            Verbal Reports from the Director of BMSU and Named Persons

*Report from the Director of BMSU:*

- The additional Home Office Inspector recently assigned to the University is working through the backlog of applications and the situation with regards to delays is improving. The Inspector

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will also be holding surgeries to provide guidance for new applicants.

- The Director of BMSU has recently met with the new Head of the University's Institute for Genomics and Cancer Sciences, who is joining Birmingham from another institution and who will be continuing his ongoing animal research here – his existing Project Licence will be considered during the current meeting.
- There is ongoing recruitment activity within the University for new Birmingham Fellows. This has prompted discussion of a wider concern about the need to involve the Director of BMSU at the earliest stages when appointing new members of staff who are planning to undertake animal research. This has been flagged at senior level within the Colleges and at the BMSU Strategic Group, as the work which new staff may wish to undertake could have considerable financial, staffing and facilities-related implications; indeed, some work may not be possible at all within BMSU. This issue will be flagged with the University's HR team so that it can be considered by Colleges as part of their long-term planning.

### *Report from the Named Veterinary Surgeon (NVS):*

- It was reported that BMSU's procedures for taking animals into quarantine when bringing them in from other institutions is working as intended, as it has recently identified infection in some such animals at the earliest stage thereby preventing its spread.

### *Report from the Named Animal Care and Welfare Officers:*

No items to report.

17/05-06

### Report from the Fast Track Procedure

The fast track procedure is up-to-date.

17/05-07-1

### Application Ref TBA – Determining dynamic changes in tumour infiltrating lymphocytes to enhance checkpoint blockade therapies

The overall aim of this project is to provide fundamental new information on the movement of immune cells into and out of tumours and how the cells change over time.

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The PI gave a presentation explaining the application to the Committee.

Much of the early work on this project will be done using tumour cell lines. Two primary tumour models (already used elsewhere) may be established at a later date, depending upon the results of the initial work with cell lines.

It was explained that the majority of patients do not currently respond to checkpoint therapies and that the combination of different such therapies may represent more effective treatments.

The majority of the experiments with tumour cell lines will only run for 3-4 weeks but experiments involving primary tumours may need to run over a longer timescale.

It was noted that little information about the 3Rs had been provided, and the PI explained that as these models are new them, the level of detail they can provide on the 3Rs at this stage is limited. In relation to the 3Rs, the PI explained that they will collaborate with experts working on similar models, will use established cell lines and established regimes and will minimise the number of animals to be used. It is likely that further refinements will be identified as the work progresses. It should be stated in the application that the NC3R's Experimental Design Assistant has been used, although it was noted that the studies are not blinded and that the mice will not be randomised.

All of the cell lines to be used have already been used elsewhere in pre-clinical models and there will be information available on their adverse effects (e.g. ulceration) which the PI will draw upon.

The Committee queried whether specialist statistical advice had been obtained. The PI explained that statistical advice was obtained when related work was first undertaken and that the statistical power calculations included in the current application draw upon studies undertaken since then. It was noted that an increase in the group size from 5 to 7 has increased the statistical confidence to 95%. The PI was advised to seek further statistical advice if required, and to state that this will be the case in the application.

It was queried why the stated number of 2500 mice is so high and the PI clarified that it is probably an over-estimate; a typical experiment will involve 2 groups of 7 mice, and will usually be repeated once or twice. Mice will be used as they are bred.

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A CRUK grant application has been submitted for the work covered by this licence – currently, all of the PI's work is covered by his Wellcome Trust Senior Fellowship.

It was queried whether there are any particular difficulties envisaged in relation to carrying out surgery on mice with tumours. The PI explained that they will try to label the tissue through the skin with a laser in order to avoid surgery; however, it was noted that labelling through the skin only has a partial effect and will still require anaesthesia. Also, the degree of pigmentation and the size of the tumour will influence the success of such labelling as these factors will affect how much light can get through. The PI was asked whether labelling through the skin on more than one occasion had been considered, and they explained that it had not and that they were uncertain what effect this might have on the data. It was noted that surgery on animals with tumours does already take place within BMSU and prior experience has shown that healing may be adversely affected – this will be addressed via the humane endpoints.

It was agreed that the scope of the application should be closely defined, with the possibility of amendments being submitted in the future if necessary.

As the labelling only lasts for a few days, it is expected to have minimal effect upon the animals.

The industrial collaborator from whom the checkpoint inhibitors will be obtained has already run toxicology tests. If new combinations of checkpoint inhibitors will be used in later studies, it is anticipated that the collaborator will run further toxicology tests for these. This should be clarified in the licence application, as toxicology testing will not be done within BMSU.

Where possible the Workman guidelines will be followed in relation to tumours and advice has been obtained from the NC3Rs on this. Volume may be used rather than linear measurements of tumours, where appropriate.

As skin does not usually form discrete tumours, it was queried how skin tumours would be measured. An existing model used elsewhere will be adopted for this and appropriate humane endpoints will be identified and specified in the licence.

A number of the humane endpoints need further consideration and revision in the application before it is submitted.

No breeding or maintenance of animals is included as all such work will be carried out under the BMSU service licence.

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After the PI left the meeting, the Committee continued its discussions.

The Committee observed that the work is preliminary in nature, particularly as none of the models have been published and neither the PI nor BMSU has previously used them. It was suggested that the number of animals should be reduced and/or the primary tumour model should be removed at this early stage, with the option of submitting amendments to cover additional work in the future if needed. This will be discussed further with the Home Office Inspector.

It was observed that many of the experiments are 'self-limiting', in that they would not progress beyond a stated point unless certain criteria are met. This should be made clear in the application and it was felt that a 'step' diagram or flow chart would be helpful in relation to this.

*Resolved that:*

The revisions discussed above will be made and feedback will be obtained from the Home Office Inspector and incorporated into the application. Once the Chair is happy with the changes, a recommendation will be made that the Establishment Licence Holder submits the application to the Home Office.

17/05-07-2

Granted PPL transfer to Birmingham – 'Models of intestinal and genetically related tumours'

It was explained that the PI of this previously granted Project Licence is moving to the University of Birmingham from another institution. Such transfers are usually dealt with via BERSC's fast track procedure, but in this case the Committee is being asked to consider the Licence as it may be appropriate to amend some elements before the work commences at Birmingham. The PI was not present for this meeting.

As there are no animal MRI facilities here, secondary availability for MRI work will have to be retained at the original institution. If some of the procedures will take place at the original institution, the PI will be required to maintain records for both establishments. It was also noted that as some of the PI's research group are not moving with him to Birmingham, secondary availability will be required for them to continue their work until they can apply for their own Project Licences.

Local controls will be necessary in relation to some of the stated humane endpoints, and these will need to be stated in the Project Licence. The NVS expressed concerns with the endpoints as currently written as they are inconsistent with those currently used within BMSU and are in some cases unclear. The endpoints may have been refined

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over time, and if this is the case it should be reflected in the Project Licence.

The Director of BMSU will clarify the number of animals with the PI, as the numbers in the application differ from the numbers quoted during earlier discussions. Work under the Project Licence has already reached the halfway point, and the numbers required are likely to be much lower than those stated.

With regards to breeding, the PI will be bringing some colonies with him to Birmingham and some will be frozen down.

The PI will be encouraged to rewrite and resubmit the Project Licence at the earliest opportunity, in the style preferred by the Home Office Inspectors assigned to Birmingham. The current style of the Licence will make it complicated to manage within BMSU, although it was emphasised that BMSU has considerable experience of managing and monitoring intestinal tumour models. It was felt that this Project Licence illustrates the wide variations between the styles of writing and structures preferred by different Home Office Inspectors.

It was suggested that it would be helpful to rewrite the protocols to be site-specific, i.e. to separate out the work to be done at each institution within different protocols.

There is no flat-bed X-ray within BMSU, meaning that whole body irradiation will have to be used instead of irradiating smaller areas of the body. It will not be possible to carry out therapeutic irradiation within BMSU. It was highlighted that the lack of X-ray facilities may be a significant limitation for the proposed work and some elements of the current Project Licence may be impossible to carry out.

All of the proposed changes will be discussed further with the Home Office Inspector, the Named Persons and the researchers who will actually be carrying out the experiments.

*Resolved that:*

The revisions discussed above will be made and feedback will be sought from the Home Office Inspector and incorporated into the Project Licence. The revised Licence will be circulated to the Committee and once the Committee is happy with the changes, a recommendation will be made that the Establishment Licence Holder submits the changes to the Home Office.

17/05-08

Matters relating to the 3Rs

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### *Joint 3Rs day*

Efforts are being made to encourage attendance at the planned 3Rs day on 19<sup>th</sup> September 2017.

### *3Rs Summer School*

It reported that up to 5 places are available for Birmingham PhD students to attend a 3Rs Summer School and members of BERSC were invited to nominate suitable students.

### *Meeting on single housing and related refinements*

The NVS reported that he recently presented at a meeting on single housing and related refinements at the University of Nottingham. Attendance at the meeting was good and the material was well-received.

### *NC3Rs Midland Programme Manager meeting with researchers*

NC3Rs Midland Programme Manager is meeting with research groups at Birmingham to encourage the sharing best practice in relation to the 3Rs.

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17/05-09

Any Other Business

Consideration is being given to the idea of including video clips of BMSU facilities on the University's webpages.

The first retrospective assessment reports (for severe Project Licences) have been submitted to the Home Office.

17/05-11

Date of Next Meeting

The date of the next meeting is 6<sup>th</sup> July 2017.



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### **GLOSSARY**

3Rs	Replacement, Reduction and Refinement
BERSC	Biomedical Ethical Review Sub-Committee
BMSU	Biomedical Services Unit
CRUK	Cancer Research United Kingdom
HR	Human Resources
MRI	Magnetic Resonance Imaging
NC3Rs	National Centre for the Replacement, Refinement and Reduction of Animals in Research
NVS	Named Veterinary Surgeon
PI	Principal Investigator
SOP	Standard Operating Procedure
TBA	To Be Announced